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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/500,832	01/06/2005	Frank Karlsen	B0192.70051US00	8927

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WOLF GREENFIELD & SACKS, P.C.
600 ATLANTIC AVENUE
BOSTON, MA 02210-2206

EXAMINER	
BABIC, CHRISTOPHER M	
ART UNIT	**PAPER NUMBER**
1637	

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10/18/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/500,832	KARLSEN, FRANK	
	Examiner	Art Unit	
	Christopher M. Babic	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 July 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-6,20 and 21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-6,20 and 21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

Claim(s) 1, 3-6, 20 and 21 are pending. The following Office Action is in response to Applicant's response dated July 27, 2007.

Sequence Rules Compliance

In view of Applicant's amendment to the specification, the instant application now complies with the Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures set forth in 37 C.F.R. §§ 1.821-1.825

Withdrawn Claim Rejections - 35 USC § 112 - Indefiniteness

Applicant's arguments, see pg. 26 section (a), filed July 27, 2007, with respect to the term --high risk-- have been fully considered and are persuasive. Thus, the rejection has been withdrawn.

The rejection of claim(s) 1-9 and 13-19 has been withdrawn in view of Applicant's amendment.

Withdrawn Claim Rejections - 35 USC § 112 – Scope of Enablement

The rejection of claim(s) 1-9 and 13-19 has been withdrawn in view of Applicant's amendment.

New Grounds of Claim Rejections - 35 USC § 103

The following new grounds of rejections are made in view of Applicant's amendment.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

1. Claim(s) 1-9 and 13-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lorincz (WO 99/29890 A2; 17 June 1999).

With regard to claim(s) 1 and 2, Lorincz teaches methods for assessing the risk of a patient with HPV to develop an HPV-based disease, e.g. the risk of a patient with HPV to develop malignant cancer (pg. 4-5, for example). Lorincz expressly teaches that the expression levels of E6 oncoproteins encoded by high-risk HPV types are a more sensitive and accurate measure of potential risk of an HPV infection developing into a cancerous lesion (pg. 7, for example). Lorincz expressly teaches an embodiment of the invention that involves the measurement of the level of expression of **ONE** or more HPV

genes discovered to be related to the stage and nature of HP-based disease (e.g. HPV E6, E7, L1, and E2) (pg. 8, for example).

Specifically, Lorincz an in vitro (pg. 11-19; example 2, for example method comprising: screening subjects (pg. 18, cell samples, for example) for expression of mRNA transcripts of the E6 gene of HPV (example 2, for example); wherein the screening for E6 mRNA expression is carried out using isothermal amplification, such as NASBA (pg. 13, for example).

Lorincz further outlines that certain HPV strains, e.g. 16 and 18 are associated with malignant cervical cancer (pg. 1-4, 7,13, for example). Lorincz does not expressly teach categorizing subjects as "high-risk" based on expression results, however, given the fact that the disclosure makes specific reference to expression levels of E6 oncoproteins encoded by high-risk HPV in combination with certain HPV strains, e.g. 16 and 18 being associated with malignant cervical cancer, Lorincz clearly suggests such a method step.

With regard to claim(s) 3 and 13, Lorincz teaches NASBA (pg. 13, for example).

With regard to claim(s) 5, 5, 15, and 16, Lorincz teaches tissue from subjects known to have malignant cervical deposits (pg. 15-16,18,23, for example).

With regard to claim(s) 7-9 and 17-19, Lorincz teaches the detection of HPV 16 (pg. 23, for example).

Thus, with regard to the above claims, based on the teachings of Lorincz, it is submitted that it would have been *prima facie obvious* to a skilled artisan at the time of

invention to screen human subjects for the expression of mRNA transcripts of the E6 gene of HPV 16 and categorize them as having a "high-risk" for developing cervical cancer.

With regard to claim(s) 20, Lorincz further outlines that certain HPV strains, e.g. 16 and 18 are associated with malignant cervical cancer (pg. 1-4, 7,13, for example). Thus, it would have been *prima facie obvious* to a skilled artisan at the time of invention to screen human subjects for the expression of mRNA transcripts of the E6 gene of HPV 18, in addition to that of HPV 16.

Response to Arguments

Applicant's arguments have been fully considered but they are not persuasive. As understood by the Examiner, Applicant argues that Lorincz does not suggest the claimed invention because the methods of Lorincz require detection of the expression of at least two genes, and assessing the stage of HPV related cancer by calculating the numeric ratio between the expression levels of the two genes. Applicant further argues that the claimed invention, in contrast to the methods according to Lorincz, there is no need for accurate quantitation of E6 expression levels, or calculation of numeric ratios, in order to practice the method of the invention. These arguments are not persuasive because first, the claimed invention does not exclude the detection of another gene and calculation of the numeric ratio between the expression levels. Applicant is reminded that the claimed invention is recited in "comprising" or "open language," which allows for the inclusion of outside steps. Furthermore, the "ratio" teaching according to Lorincz, as

understood by the Examiner, is one **embodiment** of the disclosed methods. Lorincz expressly states that, "It has been discovered that the level of expression of these genes, the ratio of expression of these genes to each other or to one or more other genes, **or both**, are indicative of the stage of HPV-based disease (pg. 8, for example)." Lorincz further teaches that, "...an increased level of expression of E6 and E7-relative to, for example, an earlier sample or a reference sample--may be indicative of high grade CIN or cancer." Thus, it is submitted that Lorincz teaches assessing cervical cancer based on the quantitation of expression levels of E6 **alone**.

Furthermore, Applicant argues that Lorincz does not contain any actual data from patient samples to substantiate that the method works in practice. This argument is not persuasive because, as highlighted by Lorincz, it was well known at the time of invention that types such as HPV 16 and18 are predominantly found in high-grade lesions and cancer, and genes E6/E7 are considered to have oncogenic activity. Furthermore, Lorincz demonstrates that different stages of HPV infection possess different ratios of gene expression (pg. 24, table 2, for example).Thus, a skilled artisan at the time of invention would have expected the methods of Lorincz to work in patient practice.

Thus, the rejections are maintained.

2. Claim(s) 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lorincz (WO 99/29890 A2; 17 June 1999) as applied to claim(s) 1, and in further view of Hendricks et al. (U.S. 5,580,970).

The teachings of the previously applied reference(s) have been outlined in the above rejections. The previously applied reference(s) do not expressly teach detection of the E6 gene of HPV type 52.

It is submitted that it was well known in the art at the time of invention that HPV 52 is associated with cervical neoplasia as demonstrated by Hendricks (col. 1, lines 15-45, 60-65, for example).

Thus, it would have been *prima facie obvious* to a skilled artisan at the time of invention to screen human subjects for the expression of mRNA transcripts of the E6 gene of HPV 52, in addition to that of HPV 16.

Conclusion

Claim(s) 1, 3-6, 20 and 21 are rejected. No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not

mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher M. Babic whose telephone number is 571-272-8507. The examiner can normally be reached on Monday-Friday 7:00AM to 4:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Christopher M. Babic
Patent Examiner
Art Unit 1637
Technology Center 1600

10/10/07

KENNETH R. HORLICK, PH.D
PRIMARY EXAMINER

10/15/07